# Multiple Sclerosis: Symptoms & Pathophysiology

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***Abstract— Multiple sclerosis is a chronic disease that affects the Central Nervous System. It is neurodegenerative disease affecting young adults mostly. And this disease is influenced by gender, genetic and environmental factors, which caused by aberrant immune activation resulting in damage to myelin sheath within the brain, spinal cord and axons. It has complex etiology involving both genetic and environmental factors. MS was first described by French neurologist Jean Martin Charcot. This is t cell mediated by autoimmune disease. This disease gradually lead to hyper phosphorylation of tau protein.***

***Index Terms— Neurological disease, Parenchymal infiltrates, Subsection edema, Epstein-Barr virus (EBV), autoimmune disease.***

## I. INTRODUCTION

What is Multiple Sclerosis?

Multiple sclerosis is chronic disease that affects the central nervous system. Especially the brain, spinal cord, also optic nerves. It is not possible to predict how multiple sclerosis will progress in any individual. According to the National Institute for Neurological Disorders and stroke (NINDS), 250,000-350,000 people in the United States are living with multiple sclerosis.

In the case of Multiple sclerosis the immune system attacks the myelin sheath that surrounds and protect nerve fibres, causing inflammation. Myelin also helps the nerves to conduct electrical signals quickly and efficiently. Multiple sclerosis means scar tissue in multiple areas.

When the myelin sheath disappears or sustains damage in multiple areas, it leaves a scar, or sclerosis. They mainly affect the –

The brain stem

The cerebellum, which coordinates movement and controls balance

- The spinal cord
- The optical nerves
- White matter in some regions of the brain

As more lesions develop, nerves fibres can break or became damaged. Therefore the electrical impulses from the brain do not flow smoothly to the target nerve. This means that the body cannot carry out functions.

## II. TYPES OF MULTIPLE SCLEROSIS

There are four types of multiple sclerosis following as;

Clinically isolated syndrome (CIS): This is a single, first episode, with symptoms lasting at least 24 hours. If another episode occurs at a later date, a doctor will diagnose relapse-remitting MS.

Relapse-remitting MS (RRMS): This is the most common form, affecting around 85% of people with MS. RRMS involves episodes of new or increasing symptoms, followed by periods of remission, during which symptoms go away partially or totally.

Primary progressive MS (PPMS): Symptoms worsen progressively, without early relapses or remissions. Some people may experience times of stability and

periods when symptoms worsen and then get better. Around 15% of people with MS have PPMS.

Secondary progressive MS (SPMS): At first, people will experience episodes of relapse and remission, but then the disease will start to progress steadily.

Multiple sclerosis signs and symptoms may differ greatly from person to person and over the course of the disease depending on the location of affected nerve fibers. Symptoms often affect movement.

## III. PATHOPHYSIOLOGY OF MULTIPLE SCLEROSIS

MS refers to the plaques that form in the CNS combined with inflammation, demyelination, axonal injury and axonal loss. These plaques are found in the brain and spinal cord, essentially in the white matter around the ventricles, optic nerves and tracts, corpus callosum, cerebellar peduncles, long tracts and subpial region of the spinal cord and brainstem, but also in the gray matter. They are expressed in all forms of MS, but vary over time quantitatively and qualitatively showing a profound heterogeneity in the structure and immunopathological patterns of demyelination and oligodendrocyte pathology between relapsing remitting course and progressive forms of disease.

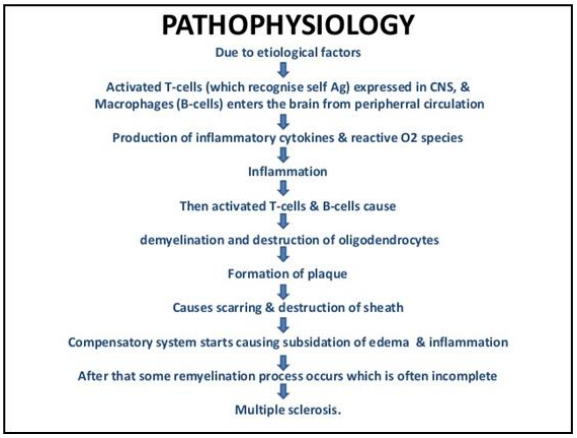
During the early stages of the relapsing remitting course, the pathology is marked by important demyelination and a variable degree of axonal loss and reactive gliosis. Patients in general, present with focal inflammatory plaques that contain demyelinated axons, reduced number of oligodendrocytes, astrocyte proliferation with subsequent gliosis, transected axons, and perivenular as well as parenchymal infiltrates of lymphocytes and macrophages. In the progressive course, MS is dominated by diffuse gray and white matter atrophy and characterized by low-grade inflammation and microglial activation at the plaque borders combined with diffuse injury of the normal-appearing white matter outside the plaque

Inflammation, microglial activation, axonal and myelin injury occurring during this course are followed by secondary demyelination. In general, the patterns of tissue injured in patients presented with primary or secondary progressive course of MS are homogeneous. They showed oligodendrocyte loss, preferential destruction of small-caliber axons, astrocytic gliosis, and demyelination that consists of the essential criteria. Demyelination and subsequent neurodegeneration associated with different forms of MS involved various components of adaptive and innate immunity. Myelin sheaths are particularly vulnerable to non-specific products, such as cytotoxic cytokines, excitotoxins, reactive oxygen or nitric oxide species, which are released by activated macrophages and microglia. However, the most commonly observed patterns of demyelination are antibody and complement-associated changes, as well as hypoxia-like tissue injury, in which the initiation of demyelination is attributed to the degeneration of distal oligodendrocyte processes and apoptosis of oligocytes, while the loss of polarity by astrocytes leads to the disturbance of the structural organizational of the perivascular glia limitans.

Classically, MS is regarded as a T cell-mediated autoimmune disorder with a predominance of CD8+ cells compared with other T-cell subsets, B cells or plasma cells. It is believed that this disease begins in inflammatory-induced lesions consisting mainly of CD8+ T cells, and CD4+ T cells, and activate microglia/macrophages.

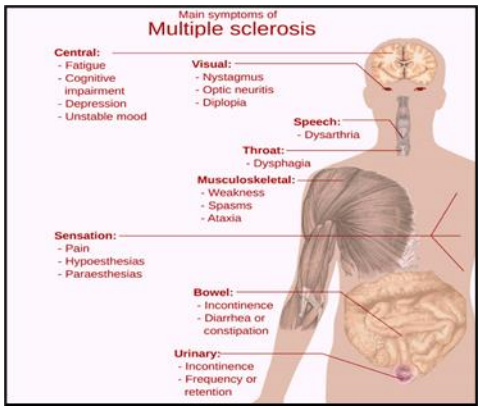
Evidence of the suppression of function that restricts CD4+ T-cell responses and the tissue-damaging role of CD8+ T cells reported to co-localize with axonal pathology have been observed. Indeed, the specific interaction of CD8+ T cells with target cells requires MHC-I expression which is tightly regulated in neurons and MHC-I molecules only in response to strong danger signals such as proinflammatory cytokines IFN-γ or TNF-α.

In short the pathophysiology can be described in flow chart;




## IV. SYMPTOMS

The most common symptoms of MS are:




- Muscle weakness: People may develop weak muscles due to lack of use or stimulation due to nerve damage.
- Numbness and tingling: A pins and needles-type sensation is one of the earliest symptoms of MS that can affect the face, body, or arms and legs.
- Lhermitte's sign: A person may experience a sensation like an electric shock when they move their neck, known as Lhermitte's sign.
- Bladder problems: A person may have difficulty emptying their bladder or need to urinate frequently or suddenly (urge incontinence). Loss of bladder control is an early sign of MS.
- Bowel problems: Constipation can cause fecal impaction, which can lead to bowel incontinence.
- Fatigue: This can undermine a person's ability to function at work or at home. Fatigue is one of the most common symptoms of MS.
- Dizziness and vertigo: These are common problems, along with balance and coordination issues.
- Sexual dysfunction: Both males and females may lose interest in sex.
- Spasticity and muscle spasms: This is an early sign of MS. Damaged nerve fibers in the spinal cord and brain can cause painful muscle spasms, particularly in the legs.
- Tremor: Some people with MS may experience involuntary quivering movements.
- Vision problems: Some people may experience double or blurred vision, a partial or total loss of vision, or red-green color distortion. This usually affects one eye at a time. Inflammation of the optic nerve can result in pain when the eye moves. Vision problems are an early sign of MS.
- Gait and mobility changes: MS can change the way people walk, because of muscle weakness and problems with balance, dizziness, and fatigue.
- Emotional changes and depression: Demyelination and nerve-fiber damage in the brain can trigger emotional changes.
- Learning and memory problems: These can make it difficult to concentrate, plan, learn, prioritize, and multitask.
- Pain: Pain is a common symptom in MS. Neuropathic pain is directly due to MS. Other types of pain occur because of weakness or stiffness of muscles.

Less common symptoms include:

- Headache
- hearing loss
- itching
- respiratory or breathing problems
- seizures
- speech disorders
- swallowing problems

There is also a higher risk of:

- urinary tract infections
- reduced activity and loss of mobility

CAUSES AND RISK FACTORS

Scientists do not really know what causes MS, but risk factors include:

- Age: Most people receive a diagnosis between the ages of 20 and 40 years.
- Sex: Most forms of MS are twice as likely to affect women as men.
- Genetic factors: Susceptibility may pass down in the genes, but scientists believe an environmental trigger is also necessary for MS to develop, even in people with specific genetic features.
- Smoking: People who smoke appear to be more likely to develop MS. They tend to have more lesions and brain shrinkage than non-smokers.
- Infections: Exposure to viruses, such as Epstein-Barr virus (EBV), or mononucleosis, may increase Trusted Source a person's risk of developing MS, but research has not shown a definite link. Other viruses that may play a role include human herpes virus type 6 (HHV6) and mycoplasma pneumonia.
- Vitamin D deficiency: MS is more common among people who have less exposure to bright sunlight, which is necessary for the body to create vitamin D. Some experts think that low levels of vitamin D may affect the way the immune system works.
- Vitamin B12 deficiency: The body uses vitamin B when it produces myelin. A lack of this vitamin may increase Trusted Source the risk of neurological diseases, such as MS.

Previous theories have included exposure to canine distemper, physical trauma, or aspartame, an artificial sweetener, but there is no evidence to support these. There is probably no single trigger for MS, but multiple factors may contribute.

DIAGNOSIS

Lesions develop as a result of damage to the myelin sheath surrounding the nerves. A spinal tap (lumbar puncture) may also need to be done.

Diagnostic testing may include the following:

MRI scan. Using a contrast dye with the MRI allows your doctor to detect active and inactive lesions throughout your brain and spinal cord.

Optical coherence tomography (OCT). In this test, a picture is taken of the nerve layers in the back of your eye to check for thinning around the optic nerve.

Spinal tap (lumbar puncture). Your doctor may order a spinal tap to find abnormalities in your spinal fluid. This test can help rule out infectious diseases. It can also be used to look for oligoclonal bands (OCBs), which can be used to diagnose MS.

Blood tests. Doctors order blood tests to help eliminate the possibility of other conditions that have similar symptoms.

Visual evoked potentials (VEP) test. This test requires the stimulation of nerve pathways to analyze electrical activity in your brain. In the past, brain stem auditory-evoked and sensory-evoked potential tests were also used to diagnose MS.

An MS diagnosis requires evidence of demyelination occurring at different times in more than one area of your brain, spinal cord, or optic nerves. Demyelination is a process that prevents nerves from efficiently sending signals.

TREATMENTS

While there's no cure for multiple sclerosis (MS), there are many treatments available. These treatments mainly focus on slowing down the progression of the disease and managing symptoms.

Disease-modifying drugs

Disease-modifying medications can reduce the frequency and severity of MS episodes, or relapses. They also can control the growth of lesions (damage to nerve fibers) and reduce symptoms.

The Food and Drug Administration (FDA) has currently approved several drugs for modifying MS. They come as:

- Injectable
- Infusions
- oral treatments

## CONCLUSION

The precise cause of MS is unknown. Nonetheless, genetic predispositions combined with environmental influences play an important role in the pathogenesis of this disease. The therapeutic effects of several agents including immunomodulation and anti-inflammatory drugs in MS have been studied. However, current treatments are not able to halt the ongoing progression of neurodegeneration. Thus, beside drug therapies, ADSCs which pursue the goals of cell transplantation may potentially provide a novel strategy for treatment of neurological diseases.

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